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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,685	03/09/2001	Gary Van Nest	377882001600	9970

25226 7590 03/22/2004

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,685	NEST ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 8-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed March 9, 2001, claims benefit to provisional application 60/188,302, filed March 10, 2000.

Applicants' amendment filed December 15, 2003, has been received and entered. Claims 1 and 7 have been amended. Claims 1-10 are pending.

Election/Restriction

Applicant's election with traverse of Group I, claims 1, 5-7 in Paper No. 12 was acknowledged.

The traversal set forth in the election was on the ground(s) that relationship of the invention is not combination-subcombination, rather it is a genus-species relationship. Applicants' arguments were not found persuasive because the specific ISS sequence set forth in claims 2-4, 8-10 do not further define only the undefined pyrimidine set forth in claims 1 and 7, because they also add other nucleic acid bases to the ends. It was noted that the different and specific nucleic acid sequences would not anticipate nor make obvious one another. Further, it was noted that specific ISS sequences known in the art have different properties based on their specific sequence. In this case, the addition of nucleotide base(s) to the ends of another sequence would produce a structurally different product and in view of the art may produce a functionally different product. The requirement was still deemed proper and is therefore made FINAL.

In the instant amendment Applicants note that the restriction requirement was made final, however maintain that the relationship of the sequences is a genus species relationship. In

particular, Applicants argue that the restriction requirement is inconsistent with the art applied in the rejection made under 35 USC 102(e). See Applicants' amendment, pages 4-5. Applicants' arguments have been fully considered but not found persuasive. It is noted that the art applied in the rejection made under 35 USC 102(e) comprises the CG pyr pyr CG sequence, however the teaching of Krieg *et al.* provides additional evidence that SEQ ID NO: 14 as well as anticipating the structural limitations of the sequence encompassed by the open language of the instant claims also has the functional properties of immunostimulating B cells as encompassed and required to practice the claimed method. More importantly, with respect to the sequences disclosed by Krieg *et al.* Table 1 serves to demonstrate that simple base pair changes and truncations can have dramatic affects on the ability of the oligonucleotide to stimulate B cell proliferation. With respect to the the sequence in claim 1 representing a genus it is maintained that claim 1 does not represent a generic claim nor is the sequence representative of a genus of sequences (except for the pyr set forth in the sequence which are currently all under examination). The sequence of claim 1 does not have all the specific limitations of the sequences in the remaining claims, for example it is not required that it has two 5' purines as set forth in claim 2. The structural search for each specific sequence would require a specific and unique search, and each sequence would require separate consideration and potentially a separate search for the functional activity associated with a given sequence. Claim 1 does not generically set forth any ISS sequence, rather a specific sequence is set forth. In this case the specific nucleotide bases are viewed as distinct elements whose specific combination provides for a specific activity. The instant situation can be compared to a complex promoter region wherein some of the sequences are required for promoter activity, some are negative regulatory elements and some are enhancer

elements. Different combinations of the promoter sequences will result in a different promoter function. Initially claiming just an enhancer element would not be considered a genus that would represent other types of promoter elements. Similarly, the addition of specific nucleotide sequences will provide different functional characteristics sometimes potentiating or abolishing the ISS activity of a given specific sequence. For the reasons above and of record, the restriction requirement is maintained. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 are pending. Claims 2-4, 8-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12. Claims 1, 5, 6 and 7 are currently under examination as they are drawn to a method of reducing severity of a symptom of a virus infection by administering the ISS 5'-C, G, pyr, pyr, C, G-3', and a kit containing said ISS sequence.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

This application contains claims drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-7 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6, 11, 14 and 15 of Application No. 09/802,686 (Pub No. US 2001/0046967).

Applicants note that the applications are commonly owned, have the same filing date and have the same claim for priority, and request that the rejection be withdrawn. See Applicants' amendment bridging pages 5-6.

Applicants' comments are noted, however the instant application and '686 have a different inventive entity. As noted in the previous office action the instant application has a different inventive entity from that of '686 (US 2001/004696A1) because it includes the additional inventor Joseph J Eiden. With respect to the claimed inventions, although the conflicting claims are not identical, they are not patentably distinct from each other because each are directed to use of the same ISS sequence for reducing the severity of a virus infection. It is noted that 09/802,686 recites treatment of a RSV infection which would anticipate the treatment of any virus as instantly claimed. It was acknowledged, as noted by Applicants', that the effective filing date March 10, 2000, is the same as the instant application but the instant application has a different inventive entity from that of US 2001/004696A1 and includes the additional inventor Joseph J Eiden. Therefore, for the reasons above and of record the rejection is maintained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 5-7 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5. 6 and 17 of Application No. 09/802,445 (Pub No. US 2001/0107212 A1) is withdrawn.

Applicants note that the applications are commonly owned, have the same filing date and have the same claim for priority, and request that the rejection be withdrawn. See Applicants' amendment bridging pages 5-6.

Review of the assignment indicates that '445 and the instant specification are commonly owned. Because the assignment, filing date and the inventive entity for both applications is the same, the provisional double patenting rejection is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5-7 stand rejected under 35 U.S.C. 102(e) as being anticipated by Krieg *et al.* (US Patent 6,218,371 B1).

Applicants initially note that the rejection appears to be in conflict with the restriction requirement. Applicants note the amendments to the claims and argue that Kreig *et al.* do not teach each and every element of the claimed invention. Specifically, Applicants argue that the teaching of Kreig *et al.* focus on the synergistic combinations of CpG oligonucleotides and cytokines. See Applicants' amendment, pages 6-7. Applicants arguments have been fully considered but not found persuasive.

It is noted that the claims as amended recite that no cytokine be administered in conjunction with administration of the CGpyr-pyrCG polynucleotide. Thus, claims 1, 5 and 6 now are drawn to a method of reducing severity of a symptom of a virus infection by administering the ISS 5'-C, G, pyr, pyr, C, G-3' excluding the addition of a cytokine, and claim 7 is drawn to a kit containing said ISS sequence that does not comprise a viral antigen nor a cytokine. As reviewed in the previous office action, Krieg *et al.* teach ISS sequences and the use of said sequences to stimulate the immune system (column 8, lines 32-45). In mammals, Krieg *et al.* teach that the ISS sequences can be used to treat viral infections (column 9, lines 6-8 and starting at line 42 through column 10). Krieg *et al.* teach various methods and among the conditions tested is the administration of the ISS sequence alone (see figures 4- 8 for example). Examiner would acknowledge that the specific experiments of Krieg *et al.* demonstrate that the addition of a cytokine provides additional benefit to providing the ISS sequence alone, however this does not take from the fact that they teach methods of providing ISS alone are also effective. At the time of filing Krieg *et al.* teach that it was known that ISS sequences and cytokines could be used to provide an immunostimulatory affect in treating a variety of conditions. Krieg *et al.* state that 'CpG oligonucleotides and immunopotentiating cytokines have the ability to produce immune responses ***on their own*** when administered to a subject' (***emphasis added*** column 6, lines 14-16). There is nothing in Krieg *et al.* that teaches that an ISS oligonucleotide sequence alone will not work, only that they work better in combination with a cytokine. Examiner would agree that at least one invention disclosed by Krieg *et al.* as set forth in the allowed claims focuses on the synergistic affect of ISS sequences and cytokines, however Krieg *et al.* also teach that at the time of filing ISS sequences alone could be used in methods wherein

immunostimulation is required for treatment. Applicants do not contest that the ISS sequence taught by anticipates the instant claims, only that Krieg *et al.* does not teach to use the sequence without a cytokine. This argument is not found persuasive because Krieg *et al.* teach that ISS sequences alone are effective immunostimulatory sequences when administered alone. Krieg *et al.* teach a variety of CpG ISS sequences and specific sequences for use in the disclosed methods, in particular specific sequences which anticipates a sequence comprising 5'-C, G, pyr, pyr, C, G-3' (see for example SEQ ID NO: 13 and 14 in Table 1).

With respect to the kit, Krieg *et al.* specifically discloses providing the materials necessary to treat an individual (see column 22, lines 27-42; and column 26, lines 40-50). In this case the instructions included as part of the kit for the use of the kit is not seen as providing patentable weight to the claimed invention for reasons of record. The CAFC in *In re Gulack* 217 USPQ 401 1983 stated that printed matter that is not functionally related to the substrate does not distinguish the invention from the prior art in terms of patentability; although printed matter must be considered, in that situation it may not be entitled to patentable weight (page 401). The court further stated that the critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate (page 404 "B"). Moreover, since ISS sequences were well known and used to stimulate the immune response to viral infections, and Krieg *et al.* specifically teach a sequence which anticipates a sequence comprising 5'-C, G, pyr, pyr, C, G-3' the claim to the kit is also anticipated.

Claims 1, 5-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Krieg *et al.* (US 2003/0050263 A1).

As above, Applicants initially note that the rejection appears to be in conflict with the restriction requirement. Applicants note the in the basis of the rejection Examiner states that Kreig *et al.* teach " the ISS sequence can be used to treat viral infections" noting that '263 is a continuation in part of the earlier application ant the paragraphs relied upon by examiner do not appear in the priority document. Accordingly '263 should be given an earlier priority date and it would not qualify as 102(e) type reference. See Applicants' amendment, pages 6 and 7. Applicants arguments have been fully considered but not found persuasive.

Initially, it is noted that Applicants do not argue that Kreig *et al.* teach the claimed invention, only that the teachings do not qualify as prior art under 35 USC 102(e). US 2003/0050263 is a continuation in part of 09/415,142 (now also US 2003/0026782) which is a divisional of 08/386,063, now US Patent 6,194,388 filed February 7, 1995. Review of both published '782 and '388 does indicate that the paragraphs indicated in the basis of the rejection are not present, as noted in Applicants arguments. However, both'728 and '388 provide clear guidance for the use of CpG sequences to fight a variety of infections including viral infection (see for example '388 column 6, lines 35-47). Moreover, the specific CpG sequences that anticipate the ISS sequence in the instant claims are also present in the '388 disclosure (see Table I). Applicants' arguments are not found persuasive because the teaching in the priority documents of '263 adequately support the instantly claimed invention, and provide the basis for the teaching of the paragraphs of '263 cited in the basis of the rejection. Though '263 is a continuation in part, review of the teachings in '263 find adequate support in the priority documents to qualify it as a 102(e) type reference.

As noted above, the claims as amended recite that no cytokine be administered in conjunction with administration of the CGpyr-pyrCG polynucleotide. Thus, claims 1, 5 and 6 now are drawn to a method of reducing severity of a symptom of a virus infection by administering the ISS 5'-C, G, pyr, pyr, C, G-3' excluding the addition of a cytokine, and claim 7 is drawn to a kit containing said ISS sequence that does not comprise a viral antigen nor a cytokine. As stated in the previous office action, Krieg *et al.* teach ISS sequences and the use of said sequences to stimulate the immune system, and in mammals, Krieg *et al.* teach that the ISS sequences can be used to treat viral infections (paragraphs 14-20). Krieg *et al.* teach various methods and among the conditions tested is the adminstration of the ISS sequence alone (see working example). Finally, Krieg *et al.* teach a variety of consensus sequences and specific sequences for use in the disclosed methods, in particular specific sequences which anticipate a sequence comprising 5'-C, G, pyr, pyr, C, G-3' (see for example SEQ ID NO: 14 and 15). Again, with respect to the kit, Krieg *et* al. specifically discloses providing the materials necessary to treat an individual. In this case the instructions for the use of the kit is not seen as providing patentable weight to the claimed invention for reasons of record. The CAFC in *In re Gulack* 217 USPQ 401 1983 stated that printed matter that is not functionally related to the substrate does not distinguish the invention from the prior art in terms of patentability; although printed matter must be considered, in that situation it may not be entitled to patentable weight (page 401). The court further stated that the critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate (page 404 "B"). Since ISS sequences were well known and used to stimulate the immune response to viral infections, and Krieg *et al.*

specifically teach a sequence which anticipates a sequence comprising 5'-C, G, pyr, pyr, C, G-3' the claim to the kit is also anticipated.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to Rene Jones at 571-272-0547.

Joseph T. Woitach